REMARKS

The Office Action has rejected Claims 1 and 3-14 under 35 U.S.C. §103(a) as defining subject matter which is allegedly rendered obvious over the teachings in U.S. Patent No. 4,666,897 to Golub et al. ("Golub et al."). In addition, the Office Action has rejected Claims 2 and 15-26 under 35 U.S.C. §103(a) as defining subject matter which is allegedly unpatentable over Golub et al. and further in view of an article by Joks et al. in J. Allergy Clin. Immunol. 1998, 101:562 ("Joks et al."). Finally, Claims 27-29 are rejected under 35 U.S.C. §103(a) as defining subject matter which is allegedly unpatentable over the teachings by Kuzin et al. in Inter Immu. 12:921-931 (2001) ("Kuzin et al.").

Applicants have amended the claims, which when considered with the comments hereinbelow, are deemed to place the present case in condition for allowance. Favorable action is respectfully requested.

Applicants have amended Claim 1 by reciting that it is directed to reducing an excessive IgE concentration in the blood of a patient which method comprises administering an IgE lowering effective amount of an antibiotic. Support for this Amendment is found on Page 6, Line 6 to Page 7, Line 3 of the instant specification. Claims 4 and 17 have been amended to correct the spelling of minocycline and to recite that a combination of antibiotics may be administered. Support for this latter amendment in Claims 4 and 17 is found on Page 6, Lines 1-10 of the instant specification. Claims 10 and 12 have been amended to be consistent with Claim 1. Support for the amendment to Claim 28 is found on Page 6, Line 29 to Page 7, Line 3 of the instant specification.

Applicants have added Claim 30 directed to the method of reducing the risk of a patient suffering from a disease in which IgE is pathogenic by administering to the patient an IgE lowering effective amount. Claim 30 recites that the concentration of IgE is less than 100 Iu/ml.

Support for Claim 30 is found on Page 16, Line 16 to Page 17, Line 3 of the instant specification.

No new matter is added to the application.

Applicants have not abandoned the deleted subject matter or any subject matter deleted from the claims and reserve the right to file the subject matter in a continuation application.

An aspect of the present invention is directed, *inter alia*, to a method for reducing excessive IgE concentrations in the blood of a patient suffering from a disease comprising administering an IgE lowering effective amount of an antibiotic composition.

Pursuant to the rejection of Claims 1 and 3-14, the Office Action cites Golub et al. Golub et al. are directed to a method of reducing pathological excess of mammalian collagenolytic enzyme activity in a mammalian system to substantially normal levels which comprises administering to a mammal in need thereof an anti-collagenolytic amount of a tetracycline which is therapeutically effective in reducing the level of collagenolytic activity substantially to normal levels. In other words, Golub et al. teach the use of a tetracycline to treat diseases or pathological states wherein excessive levels of collagenase or other collagenolytic enzymes are present. Examples of the diseases and pathological states which Golub et al. teach that the tetracyclines can treat include rheumatoid arthritis, periodontal diseases and ulcerated cornea. According to Golub et al., these disease states exhibit the pathological effects of excessive collagenase levels which include excessive resorption of bone, destruction of joint

tissue, breakdown of the gingival collagen fibers and the bone sockets and ulceration of the cornea and other destruction of collagen containing tissues. See Column 2, Lines 40-60 of Golub et al. As described therein, tetracycline serves to reduce the excessive collagenic levels and collagenaytic activity to normal levels. Golub et al. are restricted to the use of antibiotics for the reduction of excessive collagenic levels and collagenolytic activity. There is no teaching in Golub et al. that tetracycline can be used to reduce the excessive circulatory IgE concentration in the plasma of patients. A review of Golub et al. discloses that there is no mention of any IgE in the document - - let alone any teaching or suggestion that the antibiotic will lower IgE concentration in the plasma, as claimed. Moreover, the Office Action has not established a recognized nexus between the reduction of collagenic activity and IgE concentrations in the plasma.

The Office Action, however, alleges that Golub et al. disclose on Page 6, Column 2, that these antibiotics are used for the treatment of inflammation in rheumatoid arthritis or infectious periodontal disease, referring to Column 2, Lines 40-55. However, in point of fact, Golub et al. teach away from using the tetracycline for this purpose. It states specifically,

> The method of the present invention involving reducing excessive collagenolytic enzyme activity levels to normal levels can be used to treat conditions in a number of diseases, including rheumatoid arthritis, periodontal disease and ulcerated corneae. These disease states (and others) all exhibit the pathological effects of excessive collagenase levels which include excessive resorption of bone, destruction of joint tissue, breakdown of the gingival collagen fibers and the bony sockets, and ulceration of the cornea, as well as other destruction of collagen containing tissue. While other manifestations of these disease states may be treated with supplementary drugs, i.e., inflammation in rheumatoid arthritis, or infection in periodontal disease, the use of the tetracycline will

> serve to reduce the excessive collagenase levels and collagenolytic activity to a normal level...

Thus, Golub et al. suggest that drugs other than the tetracycline mentioned therein, would be used to treat inflammation in rheumatoid arthritis or infection in periodontal disease.

Consequently, Golub et al. do not teach, disclose or suggest the use of antibiotics to lower the concentration of excessive IgE in the blood, as claimed. Therefore, this rejection is obviated; withdrawal thereof is respectfully requested.

In support of the rejection of Claims 2 and 15-26, the Office Action cites Golub et al. and Joks et al.

The subject matter recited in Claims 2 and 15-26 relates to a method of treating asthma in a patient comprising administering a therapeutically effective amount of an antibiotic composition.

Applicants reiterate the comments hereinabove regarding Golub et al. Golub et al. do not teach, disclose or suggest any method of reducing the level of IgE concentration in a patient - - let alone make any determination of reducing the risk of an excessive amount of excessive IgE is pathogenic. Again, there is no mention of IgE in Golub et al. Moreover, Golub et al. do not teach, disclose or suggest those antibiotics for treating asthma. It merely relates to the use of tertracyclines for reducing collagenase or other collagenolytic enzymes.

Joks et al. report a preliminary finding that minocycline may have potential use as therapy for asthma.

The Office Action alleges that Golub et al. discloses in Column 2, Lines 40-45 that the antibiotics minocycline, doxycycline and tetracycline are used for the treatment of

inflammatory associated diseases. It alleges that Joks et al. teaches that the antibiotic minocycline is useful for the treatment of asthma and concludes that it would have been obvious to one of ordinary skill in the art at the time of the invention to use the "common treatment for inflammatory diseases disclosed by Golub et al. in the treatment of another inflammatory disease, asthma".

However, contrary to the allegations in the Office Action, Golub et al. teach away that the antibiotics are useful for the treatment of inflammation. As Golub et al. states in Column 2, Lines 40-55:

> The method of the present invention involving reducing excessive collagenolytic enzyme activity levels to normal levels can be used to treat conditions in a number of diseases, including rheumatoid arthritis, periodontal disease and ulcerated corneae. These disease states (and others) all exhibit the pathological effects of excessive collagenase levels which include excessive resorption of bone, destruction of joint tissue, breakdown of the gingival collagen fibers and the bony sockets, and ulceration of the cornea, as well as other destruction of collagen containing tissue. While other manifestations of these disease states may be treated with supplementary drugs, i.e., inflammation in rheumatoid arthritis, or infection in periodontal disease, the use of the tetracycline will serve to reduce the excessive collagenase levels and collagenolytic activity to a normal level...

Thus, Golub et al. restrict the use of tetracycline to reduce the excess collagen levels and collagenolytic activity to normal levels. They state that inflammation in rheumatoid arthritis or infection in periodontal diseases is treated with other drugs. Thus, Golub et al. teach away from the use of tetracyclines for treating inflammation in rheumatoid arthritis or infections in periodontal diseases. Thus, the underlying premise of the Office Action is incorrect. Thus,

there will be no reason for one of ordinary skill in the art to combine the teachings of the primary and secondary references.

Moreover, the combination of Golub et al. and Joks et al. does not teach, disclose or suggest that tetracyclines are useful for treating asthma. As indicated hereinabove, Golub et al. teach away from the use of tetracyclines for treating inflammatory diseases. Joks et al. does not teach that minocycline is useful for treating asthma. Even it so admits. It indicates that these findings merit further investigations into the potential use of minocyclines as therapy in asthma. After all the sample was too small to make any conclusions. Thus, it cannot be said that Joks et al. (or the combination of Joks et al.) teach, disclose or suggest the use of tetracycline for treating asthma. Moreover, there is no mention therein of IgE. Thus, the subject matter of Claims 15-26 is not taught or described or suggested in the combination of Golub et al. and Joks et al.

Moreover, with respect to Claim 2, Applicants reiterate the above commentary which is incorporated by reference. Furthermore, Joks et al. tested minocycline on patients who had moderately severe and severe steroid dependent asthma. There are several types of asthma, allergic asthma, which is the asthma recited in Claim 2, is just one kind. There is no mention therein of allergic asthma. However, even assuming, *pro arguendo*, that Joks et al. teach the use of minocycline for the treatment of severe asthma, there is no teaching or suggestion in Joks et al. as to the type of asthma being treated. Thus, the combination would not suggest that tetracyclines would be useful for treating allergic asthma. Therefore, this rejection is obviated; withdrawal thereof is respectfully requested.

Pursuant to the rejection of Claims 27-29, the Office Action cites Kuzin et al.

The subject matter in Claims 27-29 are directed to, *inter alia*, a method of monitoring the effectiveness of a drug in lowering the concentration of IgE in the plasma of a

mammal suffering from a disease in which IgE is pathogenic comprising: a) making an initial determination of the concentration of IgE in the plasma at a first time in said mammal; b)administering an effective amount of a drug which lowers IgE concentration in the plasma; c)making a determination of the concentration of IgE in the plasma at a time subsequent to the initial determination and after administration of the drug; and d) comparing the values obtained from the first and second determination wherein if the value of the second determination of the free IgE level is higher than or about the same level as the first determination and above a threshold level, then the dosage amount of the drug is increased.

The Office Action alleges that Kuzin et al. teach on Page 923 in the Results section, Paragraph 1 and 2 and in Figure 2 on Page 924, a means for monitoring the effects of doxycycline in lowering the concentration of IgE in mouse splenoytes. The Office Action alleges that the method recites the same steps as claimed.

Applicants respectfully disagree. Contrary to the allegations, the teachings in Kuzin et al. do not disclose, or suggest the present methodology. Unlike the present method, the amount of IgE is not measured in the blood plasma. But, more importantly, Kuzin et al. just compare the amount of IgE present in the supernatant before and after the administration of doxycycline. There is no teaching or suggestion of comparing the concentration to a threshold level of IgE in the plasma and there is no determination of whether the concentration of the drug administered should be increased to the patient, as claimed based upon this comparison.

Thus, Kuzin et al. do not teach, disclose or suggest all of the steps of the method. Therefore, for the reasons provided this rejection is overcome; withdrawal thereof is respectfully requested.

Therefore, in view of the amendment to the claims and the remarks herein, it is respectfully submitted that the present case is in condition for allowance; which action is earnestly solicited.

Respectfully Submitted,

Mark J. Cohen
Registration No. 32,211

SCULLY, SCOTT, MURPHY & PRESSER, P.C.
400 Garden City Plaza, Suite 300
Garden City, New York 11530
516-742-4343 - Telephone
516-742-4366 - Fax
MJC/ech